

IN THE CLAIMS:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims

1. (Currently Amended) A purified IRBIT protein (a), (b) or (c) as shown below:
 - (a) a protein (~~IRBIT~~), comprising an amino acid sequence represented by SEQ ID NO: 1,
 - (b) a protein, comprising an amino acid sequence of the 1-104 of SEQ ID NO: 1, and
 - (c) a protein, comprising an amino acid sequence derived from the amino acid sequence of SEQ ID NO: 1 or an amino acid sequence of the 1-104 of SEQ ID NO: 1, which contains a deletion, substitution or addition of at least one of amino acid residues, and binding to an IP₃ receptor.
2. (Currently Amended) A An isolated polynucleotide gene, encoding the protein of claim 1.
3. (Currently Amended) A An isolated polynucleotide gene, comprising a DNA (a), (b) or (c) as shown below:
 - (a) a DNA, comprising a nucleotide sequence of SEQ ID NO: 2,
 - (b) a DNA, comprising a nucleotide sequence of the 1 to 312 of SEQ ID NO: 2, and
 - (c) a DNA, hybridizing under stringent conditions to a DNA that is complementary to the DNA comprising the nucleotide sequence of (a) or (b), and encoding a protein that binds to the IP₃ receptor.
4. (Currently Amended) A vector, containing the gene polynucleotide of claim 2 or 3.

5. (Currently Amended) ~~The vector of claim 4, wherein a promoter is operably linked to~~ An expression vector comprising the gene polynucleotide of claim 2 or 3.

6. (Currently Amended) The vector of claim 5, wherein the ~~gene polynucleotide of claim 2 or 3~~ is linked in-frame with a gene nucleic acid molecule encoding a fluorescent protein or a photoprotein.

7. (Currently Amended) The vector of claim 6, wherein the fluorescent protein is selected from the group consisting of a green fluorescent protein (GFP), a cyan fluorescent protein (CFP), yellow fluorescent protein (YFP), Venus, and FAsH and the derivatives thereof.

8. (Currently Amended) A host cell, containing the vector of ~~any one of claims 4 to 7~~.

9. (Original) The host cell of claim 8, which is a mammalian cell.

10. (Currently Amended) An IP_3 indicator for detecting IP_3 in a sample, containing the an IRBIT protein of claim 1.

11. (Currently Amended) The IP_3 indicator of claim 10, wherein the IRBIT protein ~~of claim 1~~ is fused to a fluorescent protein or a photoprotein.

12. (Currently Amended) The IP_3 indicator of claim 11, which is used for detecting IP_3 by the FRET method using a combination of the IRBIT protein ~~of claim 1~~ labeled with one fluorescent molecule of a combination of two fluorescent molecules applicable to the FRET method, and a protein containing at least the IP_3 -binding domain of the IP_3 receptor labeled with the other fluorescent molecule of the above combination.

13. (Original) The IP_3 indicator of claim 12, wherein the combination of two fluorescent molecules is a combination of Venus and CFP, a combination of YFP and CFP, or a combination of FAsH and CFP.
14. (Original) An antibody or a functional fragment thereof, specifically recognizing the protein of claim 1.
15. (Original) The antibody or the functional fragment thereof of claim 14, which is a rabbit polyclonal antibody or a fragment thereof.
16. (Original) A method for measuring IP_3 concentration in a sample, comprising:
(i) preparing a protein complex comprising an IRBIT or a protein that contains the IP_3 receptor-binding domain of the IRBIT and a protein that contains at least the IP_3 binding domain of the IP_3 receptor,
(ii) allowing the protein complex to contact with the sample, and
(iii) quantifying a free IRBIT or a protein containing the IP_3 receptor-binding domain of the IRBIT and/or the complex.
17. (Original) The method of claim 16, wherein the quantification in (iii) above is performed utilizing an immunochemical reaction system using an anti-IRBIT antibody and/or an anti- IP_3 receptor antibody.
18. (Original) The method of claim 16 or 17, wherein the quantification in (iii) above is performed by previously labeling an IRBIT or a protein containing the IP_3 receptor-binding domain of the IRBIT or a protein containing at least the IP_3 binding domain of the IP_3 receptor, and then measuring signals originating from the labeled protein.
19. (Original) The method of claim 18, wherein the label is a fluorescent label.

20. (Original) The method of claim 16, wherein the quantification of (iii) above is performed by the FRET method.

21. (Original) The method of claim 20, which uses an IRBIT or a protein containing the IP₃ receptor-binding domain of the IRBIT labeled with YFP or Venus, and a protein containing at least the IP₃-binding domain of the IP₃ receptor labeled with CFP.

22. (Original) The method of claim 20, which uses an IRBIT or a protein containing the IP₃ receptor-binding domain of the IRBIT labeled with CFP, and a protein containing at least the IP₃-binding domain of the IP₃ receptor labeled with Venus or YFP.

23. (Original) A method for quantifying the intracellular IP₃ concentration of living cells, comprising:

(i) introducing into a cell both of a gene encoding an IRBIT or a protein containing the IP₃ receptor-binding domain of the IRBIT, labeled with one fluorescent molecule of a combination of two fluorescent molecules applicable to the FRET method, and a gene encoding a protein containing at least the IP₃ binding domain of the IP₃ receptor labeled with the other fluorescent molecule of the above combination, such that the genes can be expressed, and

(ii) irradiating the cells with the excitation wavelength of the fluorescent molecule on the lower wavelength side of the above two fluorescent molecules, and measuring under a fluorescence microscope the fluorescence wavelength of the molecule and the fluorescence wavelength of the other fluorescent molecule on the longer wavelength side.

24. (Original) The method of claim 23, wherein the combination comprising two fluorescent molecules applicable to the FRET method is a combination of Venus and CFP, a combination of YFP and CFP, or a combination of F1AsH and CFP.

25. (Original) A protein complex for quantifying IP_3 concentration, comprising an IRBIT or a protein containing the IP_3 receptor-binding domain of the IRBIT and a protein containing the IP_3 receptor or at least the IP_3 binding domain thereof.

26. (Original) A vector for quantifying intracellular IP_3 concentration of living cells, containing a gene encoding an IRBIT or a protein containing the IP_3 receptor-binding domain of the IRBIT, labeled with one fluorescent molecule of a combination of two fluorescent molecules applicable to the FRET method, and a gene encoding a protein containing at least the IP_3 binding domain of the IP_3 receptor labeled with the other fluorescent molecule of the above combination such that these genes can be expressed.

27. (Original) The vector of claim 26, wherein the combination comprising two fluorescent molecules is a combination of Venus and CFP, a combination of YFP and CFP, or a combination of F1AsH and CFP.